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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,060	07/10/2000	Neil Andrew Williams	CTH-03	6761

7590 04/21/2004

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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/600,060	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49,53-56,59-64,66,68-73,75-77 and 79-83* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49,53-56,59-64,66,68-73,75-77 and 79-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/27/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 49, 53-56, 59-64, 66, 68-69, 71-73, 75-77, and 79-83 are pending.

2. The following new ground of rejection is necessitated by the amendment filed 2/2/04.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 49, 53-56, 59-64, 66, 68-69, 71-73, 75-77, and 79-83 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for a method for treating a subject for asthma, allergic rhinitis, atoptic eczema, dermatitis, uticaria, hives comprising administering to the subject an effective amount of an agent wherein the agent is selected from the group consisting of Etx, Ctx, EtxB, and CtxB that bind to GM1 wherein the agent is administered with an allergen and is not coupled to said allergen, **does not** reasonably provide enablement for a method for treating a subject for any Type I allergy such as insect bite allergy, dietary allergy and drug allergies comprising administering to the subject a therapeutically effective amount of an agent such as Etx, Ctx, EtxB and CtxB alone that bind to GM1 or modifies any GM1 associated activity (claims 49, 53-55, 66, and 68) or with *any* antigen/allergen and not coupled to *any* antigen (claims 56, 61, 69, 71-73, 75-77, 79-83). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a method of treating asthma, allergic rhinitis, atoptic eczema, dermatitis, uticaria, hives comprising administering to the subject an effective amount of an agent wherein the agent is selected from the group consisting of Etx, Ctx, EtxB, and CtxB that binds to GM1 wherein the agent is administered *with* an allergen and is not coupled to said allergen. The specification further discloses the use of Etx, Ctx, EtxB, CtxB for screening for agent that binds to GM1 and GM1 associated activity in vitro.

The specification does not teach how to treat a subject for *any* Type I allergy such as insect bite allergy, dietary allergy and drug allergies comprising administering to the subject a therapeutically effective amount of an agent that bind to GM1 or modifies any GM1 associated activity such as Etx, Ctx, EtxB and CtxB *alone*. There is insufficient guidance and in vivo working example demonstrating that administering Etx, Ctx, EtxB or CtxB *alone* without the allergen is effective for inducing tolerance to all undisclosed antigen/allergen, drug let alone for treating all type I allergy such as asthma, allergic cough, allergic rhinitis, conjunctivitis, atopic eczema, dermatitis, uticaris, hives, inset bit allergy, dietary allergy and drug allergies.

Even if the method of treating Type I allergy by coadministering to the subject an effective amount of an agent selected from the group consisting of Etx, Ctx, EtxB, or CtxB that binds to GM1 wherein the agent is administered with an antigen/allergen and is not coupled to said antigen, there is insufficient guidance and in vivo working examples demonstrating that the claimed method is effective for treating inset bit allergy, dietary allergy and drug allergies. Further, the term "antigen" without the amino acid sequence has no structure.

Kagan *et al* teach presently, the only available treatment of food allergies is dietary vigilance and administration of self-injectable epinephrine (abstract, in particular).

Wiedermann *et al* teach suppressive versus stimulatory effects of allergen/cholera toxoid (CtB) conjugates depending on the nature of the allergen in which murine model of type I allergy as well as the route of administration (See abstract, in particular). In the absence of guidance as to the structure of "antigen/allergen", the route of immunization and in vivo working examples, it is unpredictable which undisclosed antigen/allergen when coadminister to a patient is efficacious for inducing immune tolerance.

Herz *et al* teach allergens can differ in their immunogenicity as well as in their capacity to act as tolorogens (See abstract, page 274, nature of the antigen, in particular). Herz *et al* teach until now no mouse model has been available which resembles all of human bronchial asthma (page 272, column 2, Animal models of type I allergy and asthma, in particular). Each individual

mouse strain demonstrates a unique response pattern following immunization of allergens. The same allergen causes different phenotype dependent on genetical prerequisites (page 273, column 1, in particular). Further, the route of allergen administration has important impact on the quality of the immune response (See page 273, column 2, in particular). Herz et al teach that dependence of experimental model and the antigen used, the effects as well as the mechanisms of action can vary which might indicate the complexity of predicting clinical consequences of any therapeutic approach (see page 279, in particular).

Tamura et al (of record) teach that the physical association of LTB and antigen such as OVA is required to mediate immune suppression (See page 228, column 1, Figure 2, in particular).

Further, the term "modulating" could be inhibitory or stimulatory, which actions are mutually exclusive. There is insufficient guidance as to which GM1 associated activity is stimulatory and which GM1 associated activity is inhibitory upon administering the agent to the subject, in turn, effective for treating all type I allergy.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Even if the agent is limited to Etx, there is no showing in the specification as filed that said agent could treat *all* allergic disorders such as food allergy, drug allergy, insect bites, and contact dermatitis using a model that is specific for asthma. "It is not sufficient to define the recombinant molecule by its principal biological activity, e.g. having protein A activity, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property." Colbert v. Lofdahl, 21 USPQ2d, 1068, 1071 (BPAI 1992).

For these reasons, it would require undue experimentation of even one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 2/2/04 in conjunction with the declaration under 37 C.F.R. 1.132 filed 6/13/03 by Neil Andrew Williams have been fully considered but are not found persuasive.

Applicants' position is that (1) amended claims no refer to Type I allergy only. (2) claims 49, 56, 61 and 76 have been further amended to no longer refer to antibodies, and derivatives of antibodies. (3) The declaration by Neil Andrew Williams shows working example to treating asthma, a type I allergy. As long as the specification discloses at least one method for making and using the claimed invention that bears reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied.

However, the specification does not teach how to treat a subject for *all* Type I allergy such as insect bite allergy, dietary allergy and drug allergies comprising administering to the subject a therapeutically effective amount of an agent such as Etx, Ctx, EtxB and CtxB *alone* that bind to GM1 or modified which GM1 associated activity. There is insufficient guidance and in vivo working demonstrating that administering Etx, Ctx, EtxB or CtxB *alone* without the allergen is effective for inducing tolerance to all undisclosed antigen/allergen, drug, insect bites. Even if the method of treating Type I allergy by coadministering to the subject an effective amount of an agent selected from the group consisting of Etx, Ctx, EtxB, or CtxB that binds to GM1 wherein the agent is administered with an antigen/allergen and is not coupled to said antigen, there is insufficient guidance and in vivo working examples demonstrating that the claimed method is effective for treating inset bit allergy, dietary allergy and drug allergies. Further, the term "antigen" without the amino acid sequence has no structure. Kagan *et al* teach presently, the only available treatment of food allergies is dietary vigilance and administration of self-injectable epinephrine (abstract, in particular).

Wiedermann *et al* teach suppressive versus stimulatory effects of allergen/cholera toxid (CtB) conjugates depending on the nature of the allergen in which murine model of type I allergy as well as the route of administration (See abstract, in particular). The data provided in the declaration under 37 CFR 1.132 filed 6/13/03 by Neil Andrew Williams is limited to treating asthma using only EtxB.

Herz *et al* teach allergens can differ in their immunogenicity as well as in their capacity to act as tolorogens (See abstract, page 274, nature of the antigen, in particular). Herz *et al* teach until now no mouse model has been available which resembles all of human bronchial asthma (page 272, column 2, Animal models of type I allergy and asthma, in particular). Each individual

mouse strain demonstrates a unique response pattern following immunization of allergens. The same allergen causes different phenotype dependent on genetical prerequisites (page 273, column 1, in particular). Further, the route of allergen administration has important impact on the quality of the immune response (See page 273, column 2, in particular). Herz et al teach that dependence of experimental model and the antigen used, the effects as well as the mechanisms of action can vary which might indicate the complexity of predicting clinical consequences of any therapeutic approach (see page 279, in particular). Further, the term "modulating" could be inhibitory or stimulatory, which actions are mutually exclusive. There is insufficient guidance as to which GM1 associated activity is stimulatory and which GM1 associated activity is inhibitory upon administering the agent to the subject, in turn, effective for treating all type I allergy.

5. No claim is allowed.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.

8. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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April 19, 2004

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